```
 s (tgf or tgfbeta) (5n) receptor
           95085  TGF
            5744  TGFBETA
         1994264  RECEPTOR
      S1   11862  (TGF OR TGFBETA) (5N) RECEPTOR
? s constant (5n) (immunoglobulin or IgG or Ig)
          863039  CONSTANT
          402631  IMMUNOGLOBULIN
          198354  IGG
           54839  IG
      S2    4244  CONSTANT (5N) (IMMUNOGLOBULIN OR IGG OR IG)
? s s1 and s2
           11862  S1
            4244  S2
      S3       8  S1 AND S2
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
      S4       6  RD  (unique items)
? t s4/3,k,ab/1-6

 4/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12727371   PMID: 10748032
  Transcriptional regulation of the transforming growth factor-beta -inducible mouse germ line Ig alpha constant region gene by functional cooperation of Smad, CREB, and AML family members.
  Zhang Y; Derynck R
  Departments of Growth and Development and Anatomy, Programs in Cell Biology and Developmental Biology, University of California at San Francisco, San Francisco, California 94143-0640, USA.
  Journal of biological chemistry (UNITED STATES) Jun 2 2000, 275 (22) p16979-85, ISSN 0021-9258--Print Journal Code: 2985121R
  Contract/Grant No.: CA63101; CA; NCI
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Smads regulate transcription of defined genes in response to transforming growth factor-beta ( TGF -beta) receptor activation. This process involves functional cross-talk of Smads with transcription factors at responsive DNA elements to achieve maximal transcription activation and specificity. TGF-beta has been shown to induce transcription of the germ line (GL) Ig alpha constant region gene and to direct class switching to IgA antibodies. It has been shown that acute myeloid leukemia (AML) transcription factors cooperate with Smad3 to stimulate transcription from the GL Ig alpha constant region gene promoter. We report here that the TGF-beta-induced transcription from this promoter requires DNA binding of cAMP-response element-binding protein (CREB) to the nearby ATF/cAMP-response element site and of Smads to a nearby Smad binding sequence. At these sites, Smad3/4 cooperates with CREB to activate transcription in response to TGF-beta, and disruption of either binding sequence abolished TGF-beta-induced transcription. In addition, AML1 or AML2 also binds to the promoter and cooperates with Smad3/4, and in this
```

way further enhances the TGF-beta-induced transcriptional activation of the GL Ig alpha promoter. Thus, whereas Smad3/4, CREB, and AML family members bind independently to the respective DNA sequences in the GL Ig alpha promoter, functional synergy of Smads with CREB and AML proteins results in maximal TGF-beta-induced transcription.

Transcriptional regulation of the transforming growth factor-beta -inducible mouse germ line Ig **alpha** constant **region gene by functional cooperation of Smad, CREB, and AML family members.**

Smads regulate transcription of defined genes in response to transforming growth factor-beta (**TGF** -beta) **receptor** activation. This process involves functional cross-talk of Smads with transcription factors at responsive DNA...

... and specificity. TGF-beta has been shown to induce transcription of the germ line (GL) **Ig** alpha **constant** region gene and to direct class switching to IgA antibodies. It has been shown that acute myeloid leukemia (AML) transcription factors cooperate with Smad3 to stimulate transcription from the GL **Ig** alpha **constant** region gene promoter. We report here that the TGF-beta-induced transcription from this promoter...

4/3,K,AB/2 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10964289 IFI Acc No: 2005-0203022
IFI Publication Control No: 2005-0203022 IFI Chemical Acc No: 2005-0047207
Document Type: C
TYPE II TGF **-BETA** RECEPTOR / IMMUNOGLOBULIN CONSTANT **REGION FUSION PROTEINS**
Inventors: Cate Richard (US); Gotwals Philip (US); Koteliansky Victor (US); Sanicola-Nadel Michelle (US)
Assignee: Biogen Idec Inc
Assignee Code: 66889
Attorney, Agent or Firm: Kevin J. McGough, Esquire;Coleman, Sudol & Sapone, P.C., 714 Colorado Avenue, Bridgeport, CT, 06605, US
Publication (No,Kind,Date), Applic (No,Date):
US 20050203022 A1 20050915 US 2005108597 20050418
Priority Applic(No,Date): US 2005108597 20050418; US 2000423018 20001012
Provisional Applic(No,Date): US 60-44641 19970418

Abstract: Fusion proteins comprising the **TGF** -beta Type II **receptor** linked to a portion of an **immunoglobulin constant** chain are described. Also described are methods of using the fusion proteins of the invention to treat a variety of fibroproliferative disorders.

TYPE II TGF **-BETA** RECEPTOR / IMMUNOGLOBULIN CONSTANT **REGION FUSION PROTEINS**

Abstract: Fusion proteins comprising the **TGF** -beta Type II **receptor** linked to a portion of an **immunoglobulin constant** chain are described. Also described are methods of using the fusion proteins of the invention...

Exemplary Claim:
...said individual a TGF-beta lowering amount of a TGF-beta antagonist

that is a **TGF** -beta **receptor** fusion protein comprising the sequence of amino acids of SEQ ID NOS: 8 or 9.

Non-exemplary Claims:

...condition associated with TGF-beta overproduction comprising the step of administering to the individual a **TGF** -beta Type II **receptor** fusion protein having an amino acid sequence shown SEQ ID NOS: 8 or 9 in ...

...17. The method of claim 16, wherein the **TGF** -beta **receptor** fusion protein is administered by a method selected from the group consisting of intravenous, intraocular...

4/3,K,AB/3 (Item 2 from file: 340)

Dialog Acc No: 10206873 IFI Acc No: 2002-0150580
IFI Publication Control No: 2002-0150580 IFI Chemical Acc No: 2002-0038566
Document Type: C

RECOMBINANT ANTIBODIES FOR HUMAN THERAPY; ADMINISTERING GENETIC ENGINEERED ANTIBODY; BINDING TO ANTIGEN; RHEUMATIC DISEASES, SKIN DISORDERS, AUTOIMMUNE DISEASE

Inventors: Hanna Nabil (US); Newman Roland A (US); Raab Ronald W (US)
Assignee: IDEC Pharmaceuticals Corp
Assignee Code: 40498
Attorney, Agent or Firm: PILLSBURY WINTHROP, LLP, P.O. BOX 10500, MCLEAN, VA, 22102, US

Publication (No,Kind,Date), Applic (No,Date):
US 20020150580 A1 20021017 US 2001850165 20010508
Priority Applic(No,Date): US 2001850165 20010508; US 92912292 19920710; US 95476237 19950607; US 9882472 19980521; US 91735064 19910725; US 92856281 19920323; US 95397072 19950417

Abstract: Chimeric antibodies including an Old World monkey portion and a human portion, nucleic acid encoding such antibodies, Old World monkey monoclonal antibodies, and methods for their production and use.

Exemplary Claim:

...1. A recombinant antibody comprising a human, a chimpanzee or a first Old World monkey **immunoglobulin constant** region and an antigen-binding portion of a second Old World monkey immunoglobulin variable region...

Non-exemplary Claims:

...3. A recombinant antibody comprising an **immunoglobulin constant** region which is not immunogenic to a human, a framework region which is essentially not...

...to a constant region of a human, a chimpanzee or a second old World monkey **immunoglobulin constant** region, wherein said first and second Old World monkey can be the same or different...

...10. A recombinant antibody comprising a first Old World monkey **immunoglobulin constant** region and a second antigen-binding portion of a different Old World monkey immunoglobulin variable...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD18, CD5a, CD11c, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CD5a, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CD5a, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...
...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CD5a, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CDSA, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...receptor, CD3, CD28, CD8, CD11a, CD18, CD11b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...receptor, CD3, CD28, CD8, CD18, CD11a, CD11b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD18, CD11a, CD1b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, and CD71...receptor, CD3, CD28, CD8, CD18, CD11a, CD11b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** alpha , **TGF** alpha **receptor** , PDGF, or CD71...

4/3,K,AB/4 (Item 3 from file: 340)

Dialog Acc No: 10060530 IFI Acc No: 2002-0004037
IFI Publication Control No: 2002-0004037 IFI Chemical Acc No: 2002-0000919
Document Type: C
VARIANT TYPE II TGF **-BETA** RECEPTOR **FUSION PROTEINS AND METHODS; COMPETITIVE INHIBITORS; TREAT FIBROPORLIFERATIVE DISORDERS**
Inventors: Cate Richard (US); Gotwals Philip (US); Koteliansky Victor (US); Sanicola-Nadel Michele (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Probable Assignee: Biogen Inc
Attorney, Agent or Firm: BIOGEN, INC., 14 Cambridge Center, Cambridge, MA, 02142, US
Publication (No,Kind,Date), Applic (No,Date):
US 20020004037 A1 20020110 US 2000734300 20001211
Priority Applic(No,Date): US 2000734300 20001211; WO 99US13629 19990616
Provisional Applic(No,Date): US 60-89452 19980616

Abstract: Fusion proteins comprising a variant form of **TGF** -beta Type II **receptor** linked to a portion of an **immunoglobulin constant** chain are described. Also described are methods of using the fusion proteins of the invention to treat a variety of fibroproliferative disorders.

VARIANT TYPE II TGF **-BETA** RECEPTOR **FUSION PROTEINS AND METHODS**...

Abstract: Fusion proteins comprising a variant form of **TGF** -beta Type II **receptor** linked to a portion of an **immunoglobulin constant** chain are described. Also described are methods of using the fusion proteins of the

invention...

Exemplary Claim:

1. An isolated **TGF** -beta **receptor** fusion protein that comprises a splice variant of **TGF** -beta **receptor** , the fusion protein competitively inhibiting binding of **TGF** -beta to **TGF** -beta **receptor** .

Non-exemplary Claims:

2. The fusion protein of claim 1, comprising the splice variant of **TGF** -beta Type II **receptor** linked to a second protein that is not a **TGF** -beta **receptor** .

...

...3. The fusion protein of claim 2, wherein the second protein is a **constant** region of an **immunoglobulin** .

...

...5. An isolated **TGF** -beta **receptor** fusion protein encoding, on expression, for a polynucleotide sequence comprising SEQ ID NO: 1...

...6. The isolated **TGF** -beta **receptor** fusion protein of claim 5, comprising SEQ ID NO: 2...

...7. An isolated polynucleotide encoding, on expression, for a splice variant form of **TGF** -beta Type II **receptor** linked to a second protein that is not a **TGF** -beta **receptor** .

...

...9. A composition comprising a splice variant form of **TGF** -beta **receptor** fusion protein comprising SEQ ID NO: 2 in a pharmaceutically acceptable carrier, the fusion protein...

...12. A method for producing a variant form of **TGF** -beta **receptor** fusion protein, comprising culturing the host cell of claim 11, allowing said cell to express...

...said individual a TGF-beta-lowering amount of a TGF-beta antagonist that is a **TGF** -beta **receptor** fusion protein comprising amino acid residues 1 to 185 of SEQ ID NO: 2...

...administering to said individual an effective amount of a TGF-beta antagonist that is a **TGF** -beta **receptor** fusion protein comprising amino acids 1 to 185 of SEQ ID NO: 2...

...condition associated with TGF-beta overproduction comprising the step of administering to the individual a **TGF** -beta Type II **receptor** fusion protein comprising amino acids 1 to 185 of SEQ ID NO: 2...

...16. The method of claim 15, wherein the **TGF** -beta **receptor** fusion protein is administered by a method selected from the group consisting of intravenous, intraocular...

...a fibrotic condition associated with restenosis, comprising the step of administering to the individual a **TGF** -beta Type II **receptor** fusion protein having an amino acid sequence comprising amino acids 1 to 185 of SEQ

4/3,K,AB/5 (Item 4 from file: 340)

DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2913778 IFI Acc No: 9735086
IFI Publication Control No: 9735086
Document Type: C
RECOMBINANT ANTIBODIES FOR HUMAN THERAPY; NUCLEIC ACID SEQUENCE ENCODING OLD WORLD MONKEY IMMUNOGLOBULIN-BINDING REGION AND SECOND SEQUENCE ENCODING HUMAN OR CHIMPANZEE REGION
Inventors: Hanna Nabil (US); Newman Roland A (US); Raab Ronald W (US)
Assignee: IDEC Pharmaceuticals Corp
Assignee Code: 40498
Document Type: REASSIGNED
Attorney, Agent or Firm: Burns, Doane, Swecker & Mathis, LLP
Publication (No,Kind,Date), Applic (No,Date):
US 5693780 A 19971202 US 95481869 19950607
Calculated Expiration: 20141202
Priority Applic(No,Date): US 95481869 19950607; US 92912292 19920710; US 91735064 19910725; US 92856281 19920323; US 95379072 19950125

Abstract: Chimeric antibodies including an Old World monkey portion and a human portion, nucleic acid encoding such antibodies, Old World monkey monoclonal antibodies, and methods for their production and use.

Exemplary Claim:
...World monkey immunoglobulin antigen-binding region and (ii) a second nucleic acid sequence encoding an **immunoglobulin constant** region selected from group consisting of human **immunoglobulin constant** region and chimpanzee **immunoglobulin constant** region.
Non-exemplary Claims:
...receptor, CD3, CD28, CD8, CD11a, CD11b, CD18, CD5a, CD11c, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD18, CD5a, CD11c, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

4/3,K,AB/6 (Item 5 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2873822 IFI Acc No: 9722647
IFI Publication Control No: 9722647
Document Type: C
RECOMBINANT ANTIBODIES FOR HUMAN THERAPY; INCLUDES AN OLD WORLD MONKEY PORTION AND A HUMAN PORTION, NUCLEIC ACID ENCODING SUCH ANTIBODIES
Inventors: Hanna Nabil (US); Newman Roland A (US); Raab Ronald W (US)
Assignee: IDEC Pharmaceuticals Corp
Assignee Code: 40498
Document Type: REASSIGNED
Attorney, Agent or Firm: Burns, Doane, Swecker & Mathis
Publication (No,Kind,Date), Applic (No,Date):
US 5658570 A 19970819 US 95379072 19950125
Calculated Expiration: 20140819

(Cited in 006 later patents)
Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 20010327
Priority Applic(No,Date): US 95379072 19950125; US 92912292 19920710; US 91735064 19910725; US 92856281 19920323

Abstract: Chimeric antibodies including an Old World monkey portion and a human portion, nucleic acid encoding such antibodies, Old World monkey monoclonal antibodies, and methods for their production and use.

Exemplary Claim:

D R A W I N G

1. A chimeric antibody comprising an **immunoglobulin constant** region and an antigen binding region, said **immunoglobulin constant** region being selected from the group consisting of human **immunoglobulin constant** region and chimpanzee **immunoglobulin constant** region, and said antigen binding region being an Old World Monkey antigen-binding region.

Non-exemplary Claims:

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD18, CD5a, CD11c, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CD5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CD5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...receptor, CD3, CD28, CD8, CD18, CD11a, CD11b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD18, CD11a, CD11b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, or CD71...

? log off

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            $0.22  1 Types
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     $1.33  Estimated cost File434
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           $15.65  5 Types
    $21.26  Estimated cost File340
            OneSearch, 5 files,  1.165 DialUnits FileOS
     $0.80  TELNET
    $32.00  Estimated cost this search
    $32.05  Estimated total session cost   1.376 DialUnits
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Logoff: level 05.12.03 D 12:12:42

You are now logged off

ialog Acc No: 10360208 IFI Acc No: 2003-0104625
IFI Publication Control No: 2003-0104625 IFI Chemical Acc No: 2003-0029677
Document Type: C
NOVEL ONCOLYTIC ADENOVIRAL VECTORS; GENE THERAPY; ANTITUMOR AGENTS; ANTIPROLIFERATIVE AGENTS
Inventors: Cheng Cheng (US); Clarke Lori (US); Connelly Sheila (US); Ennist David Leonard (US); Forry-Schaudies Suzanne (US); Gorziglia Mario (US); Hallenbeck Paul L (US); Hay Carl M (US); Jakubczak John Leonard (US); Kaleko Michael (US); Phipps Sandrina (US); Police Seshidhar Reddy (US); Ryan Patricia Clare (US); Stewart David A (US); Xie Yuefeng (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Probable Assignee: Cell Genesys Inc
Attorney, Agent or Firm: THOMAS HOXIE NOVARTIS CORPORATION, PATENT AND TRADEMARK DEPT, 564 MORRIS AVENUE, SUMMIT, NJ, 079011027
Publication (No,Kind,Date), Applic (No,Date):
US 20030104625 A1 20030605 US 200281969 20020222
Priority Applic(No,Date): US 200281969 20020222
Provisional Applic(No,Date): US 60-270922 20010223; US 60-295037 20010601; US 60-348670 20020114
Abstract: The present invention relates to oncolytic adenoviral vectors and their use in methods of gene therapy. Provided is a recombinant **viral** vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: A left ITR, a termination signal sequence, an E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant **viral** vector, an adenoviral packaging signal, and a right ITR.

Abstract: ...oncolytic adenoviral vectors and their use in methods of gene therapy. Provided is a recombinant **viral** vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential...

...responsive promoter which is operably linked to a gene essential for replication of the recombinant **viral** vector, an adenoviral packaging signal, and a right ITR.

Exemplary Claim:

D R A W I N G

1. A recombinant **viral** vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential...

...responsive promoter which is operably linked to a gene essential for replication of the recombinant **viral** vector, an adenoviral packaging signal, and a right ITR.

Non-exemplary Claims:

2. The recombinant **viral** vector of claim 1, wherein the termination signal sequence is the SV40 early polyadenylation signal...

...3. The recombinant **viral** vector of claim 1, wherein the E2F responsive promoter is the human E2F-1 promoter...

...4. The recombinant **viral** vector of claim 1, wherein the adenoviral nucleic acid backbone is derived from adenovirus serotype...

...5. The recombinant **viral** vector of claim 1, wherein the gene essential

for replication is the E1A gene...

...6. The recombinant **viral** vector of claim 1, further comprising a deletion upstream of the termination signal sequence...

...7. The recombinant **viral** vector of claim 6, further comprising a deletion between nucleotides 103 and 551 of the...

...8. The recombinant **viral** vector of claim 1, further comprising a mutation or deletion in the E3 region...

...9. The recombinant **viral** vector of claim 5, further comprising a tissue-specific promoter operably linked to E4...

...10. The recombinant **viral** vector of claim 9, wherein said tissue-specific promoter is derived from the human telomerase...

...11. The recombinant **viral** vector of claim 9, wherein said tissue-specific promoter is the Trtex promoter SEQ ID...

...12. The recombinant **viral** vector of claim 9, which is the Ar17pAE2fFTrtex vector...

...13. The recombinant **viral** vector of claim 9, wherein said tissue-specific promoter is derived from the osteocalcin promoter...

...14. The recombinant **viral** vector of claim 8, wherein the E3 region has been deleted from said backbone...

...15. The recombinant **viral** vector of claim 1, which is the Ar6pAE2fF vector, or the Ar35E2FE1a vector...

...16. The recombinant **viral** vector of claim 1, further comprising a mutation or deletion ...17. The recombinant **viral** vector of claim 16, wherein said mutation or deletion results in the loss of the...

...18. The recombinant **viral** vector of claim 1, further comprising a therapeutic gene...

...19. The recombinant **viral** vector of claim 18, wherein said therapeutic gene is inserted in the E3 region...

...20. The recombinant **viral** vector of claim 19, wherein said therapeutic gene is inserted in place of the 19...

...21. The recombinant **viral** vector of claim 18, wherein said therapeutic gene is an immunostimulatory gene...

...22. The recombinant **viral** vector of claim 21, wherein said immunostimulatory gene is a cytokine...

...23. The recombinant **viral** vector of claim 21, wherein the immunostimulatory gene is selected from the group consisting of...

...24. The recombinant **viral** vector of claim 21, wherein said immunostimulatory gene is selected from the group consisting of...

...25. The recombinant **viral** vector of claim 21, wherein said immunostimulatory gene is a tumor associated antigen...

...26. The recombinant **viral** vector of claim 25, wherein said tumor associated antigen is selected from the group consisting...

...27. The recombinant **viral** vector of claim 21, wherein said immunostimulatory gene is an antibody that blocks inhibitory signals...

...28. The recombinant **viral** vector of claim 27, wherein the inhibitory signal is due to expression of CTLA4...

...29. The recombinant **viral** vector of claim 18, wherein the therapeutic gene is an anti-angiogenic gene30. The recombinant **viral** vector of claim 29, wherein said anti-angiogenic gene is selected from the group consisting...

...31. The recombinant **viral** vector of claim 29, wherein said anti-angiogenic gene is an **inhibitor** of PDGF, **TGF** beta , or IGF-1...

...32. The recombinant **viral** vector of claim 29, wherein said anti-angiogenic gene is a fragment of an extracellular...

...33. The recombinant **viral** vector of claim 32, wherein said extracellular matrix protein is selected from the group consisting of angiostatin, endostatin, kininostatin, fibrinogen-E, **thrombospondin** , tumstatin, canstatin, and restin...

...34. The recombinant **viral** vector of claim 29, wherein the anti-angiogenic gene is a fragment of TrpRS...

...35. The recombinant **viral** vector of claim 29, wherein the anti-angiogenic gene is selected from the group consisting...

...36. The recombinant **viral** vector of claim 18, wherein said therapeutic gene is a suicide gene...

...37. The recombinant **viral** vector of claim 36, wherein said suicide gene is selected from the group consisting of...

...38. The recombinant **viral** vector of claim 1, wherein said recombinant **viral** vector is capable of selectively replicating in and lysing Rb-pathway defective cells...

...39. The recombinant **viral** vector of claim 38, wherein tumor-selectivity is at least about 3-fold as measured...

...40. A recombinant **viral** vector comprising an Ad5 nucleic acid backbone, wherein said backbone comprises in sequential order: a...

...41. The recombinant **viral** vector of claim 40 further comprising a deletion between nucleotides 103 and 551 of the...

...42. The recombinant **viral** vector of claim 40 further comprising a mutation or deletion in the E1b gene, wherein...

...43. The recombinant **viral** vector of claim 40, further comprising a tissue-specific promoter operably linked to E4...

...44. The recombinant **viral** vector of claim 43, wherein said tissue-specific promoter is derived from the human telomerase...

...45. The recombinant **viral** vector of claim 43, wherein said

tissue-specific promoter is the Trtex promoter...

...46. The recombinant **viral** vector of claim 43, which is the Ar17pAE2fFTrtex vector...

...47. The recombinant **viral** vector of claim 43, wherein said tissue-specific pro

```
? ds

Set     Items   Description
S1      23006   (BLOCK? OR ANTAGON? OR NEUTRALI? OR INHIBIT? OR DOWN?) (5N-
             )TGF?
S2       9859   THROMBOSPONDIN
S3        282   S1 AND S2
S4        138   RD  (unique items)
? s virus or viral
         1246827  VIRUS
          743475  VIRAL
      S5 1479296  VIRUS OR VIRAL
? s ?virus or ?viral
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               0  ?VIRAL
      S6       0  ?VIRUS OR ?VIRAL
? s s4 and s5
             138  S4
         1479296  S5
      S7       8  S4 AND S5
? t s7/3,k,ab/1-8

 7/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
```

```
 s (TGF? or tgfbeta) (5n)receptor
          103299  TGF?
            5744  TGFBETA
         1994264  RECEPTOR
      S1   12346  (TGF? OR TGFBETA) (5N)RECEPTOR
? s fc (5n) (fused or fusion or conjugat? or chimer?)
           74685  FC
          133532  FUSED
          378270  FUSION
          309741  CONJUGAT?
          117256  CHIMER?
      S2    5030  FC (5N) (FUSED OR FUSION OR CONJUGAT? OR CHIMER?)
? s s1 and s2
           12346  S1
            5030  S2
      S3      67  S1 AND S2
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
      S4      27  RD  (unique items)
? s s4 and py<=1997
Processing
              27  S4
        33362888  PY<=1997
      S5       1  S4 AND PY<=1997
? t s5/3,k,ab/1

 5/3,K,AB/1     (Item 1 from file: 55)
DIALOG(R)File  55:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.

0010676173   BIOSIS NO.: 199799310233
Gene therapy by  TGF -beta- receptor -IgG  Fc   chimera  inhibited
  extracellular matrix accumulation in experimental glomerulonephritis
AUTHOR: Isaka Yoshitaka (Reprint); Akagi Yoshitaka; Kaneda Yasumi; Yamauchi
  Atushi; Orita Yoshimasa; Ueda Naohiko; Imai Enyu
AUTHOR ADDRESS: Osaka Univ., Osaka, Japan**Japan
JOURNAL: Journal of the American Society of Nephrology  7 (9): p1735 1996
1996
CONFERENCE/MEETING: 29th Annual Meeting of the American Society of
Nephrology  New Orleans, Louisiana, USA  November 3-6, 1996; 19961103
ISSN: 1046-6673
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

Gene therapy by  TGF -beta- receptor -IgG  Fc   chimera  inhibited
  extracellular matrix accumulation in experimental glomerulonephritis
 1996
DESCRIPTORS:
  MISCELLANEOUS TERMS:    ...TRANSFORMING GROWTH FACTOR-BETA TYPE II
    RECEPTOR-IMMUNOGLOBULIN G- FC   CHIMERA ;
?
```

18/3,K,AB/4 (Item 3 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2869025 IFI Acc No: 9721515
IFI Publication Control No: 9721515
Document Type: C
PROTECTION AGAINST LIVER DAMAGE BY HGF; MOLECULE COMPRISING FIRST DOMAIN COMPRISING HEPATOCYTE GROWTH FACTOR, SECOND DOMAIN COMPRISING ACTIVIN ANTAGONIST OR TRANSFORMING GROWTH FACTOR-BETA ANTAGONIST
Inventors: Roos Filip (US); Schwall Ralph (US)
Assignee: Genentech Inc
Assignee Code: 07579
Attorney, Agent or Firm: Merchant, Gould, Smith, Edell, Welter & Schmidt
Publication (No,Kind,Date), Applic (No,Date):
US 5654404 A **19970805** US 95419654 19950410
Calculated Expiration: 20140805
(Cited in 004 later patents)
Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19980505
Priority Applic(No,Date): US 95419654 19950410; US 92968711 19921030; US 92946263 19920916; US 94310361 19940921

Abstract: The present invention provides methods for preventing occurrence or progression of liver damage using hepatocyte growth factor. In the methods, a preventatively effective amount of the hepatocyte growth factor is administered to the patient. The hepatocyte growth factor can be administered, for instance, prior to administering a hepatotoxic therapy to the patient. The hepatocyte growth factor can further be administered with activin or transforming growth factor-beta to prevent liver damage. Compositions comprising hepatocyte growth factor and activin antagonist or transforming growth factor-beta antagonist are also provided by the invention.

Publication (No,Kind,Date), Applic (No,Date):
... **19970805**
Non-exemplary Claims:
...3. The molecule of claim 2, further comprising an **immunoglobulin** sequence...

...5. The molecule of claim 1, wherein said HGF is **fused** to an **immunoglobulin** sequence...

...claim 1, wherein said molecule is a bispecific immunoadhesin comprising: an HGF amino acid sequence **fused** to an **immunoglobulin** sequence; and an activin antagonist or a TGF- Beta antagonist...
...wherein said activin antagonist or TGF- Beta antagonist comprises an antigen binding site of an **immunoglobulin** sequence...

...immunoadhesin comprises an HGF amino acid sequence and a TGF-Beta antagonist amino acid sequence **fused** to an **immunoglobulin** sequence or an HGF amino acid sequence and an activin antagonist sequence **fused** to an **immunoglobulin** sequence...

...molecule of claim 14, wherein said TGF- Beta antagonist comprises a soluble form of a **TGF** - Beta **receptor** .
...

...16. A bispecific immunoadhesin comprising HGF **fused** to an **immunoglobulin** sequence, wherein the **immunoglobulin** sequence comprises an anti-activin or anti-TGF- Beta antibody...

...17. A bispecific immunoadhesin comprising HGF and follistatin, each **fused** to an **immunoglobulin** sequence

```
? log off
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            $7.16    2.106 DialUnits File155
     $7.16  Estimated cost File155
            $4.80    0.799 DialUnits File55
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            $2.20  1 Types
     $7.00  Estimated cost File55
           $29.20    1.244 DialUnits File34
               $6.82  1 Type(s) in Format 55 (UDF)
            $6.82  1 Types
    $36.02  Estimated cost File34
           $33.15    1.413 DialUnits File434
    $33.15  Estimated cost File434
           $28.11    1.606 DialUnits File340
               $9.39  3 Type(s) in Format  5 (UDF)
            $9.39  3 Types
    $37.50  Estimated cost File340
            OneSearch, 5 files,  7.168 DialUnits FileOS
     $2.93  TELNET
   $123.76  Estimated cost this search
   $123.86  Estimated total session cost   7.379 DialUnits


Logoff: level 05.12.03 D  11:27:17


You are now logged off
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? ds

Set     Items   Description
S1      12346   (TGF? OR TGFBETA) (5N)RECEPTOR
S2       5030   FC (5N) (FUSED OR FUSION OR CONJUGAT? OR CHIMER?)
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S4         27   RD  (unique items)
S5          1   S4 AND PY<=1997
? s fc
      S6   74685  FC
? s s1 and s6
           12346  S1
           74685  S6
      S7     125  S1 AND S6
? s fused or fusion or conjugat? or chimer?
           133532  FUSED
           378270  FUSION
           309741  CONJUGAT?
           117256  CHIMER?
      S8  871554  FUSED OR FUSION OR CONJUGAT? OR CHIMER?
? s s7 and s8
             125  S7
          871554  S8
      S9      79  S7 AND S8
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
     S10      38  RD  (unique items)
? s s10 and py<=1997
Processing
              38  S10
        33362888  PY<=1997
     S11       1  S10 AND PY<=1997
? s s11 not s5
              1  S11
              1  S5
     S12       0  S11 NOT S5
? ds

Set     Items   Description
S1      12346   (TGF? OR TGFBETA) (5N)RECEPTOR
S2       5030   FC (5N) (FUSED OR FUSION OR CONJUGAT? OR CHIMER?)
S3         67   S1 AND S2
S4         27   RD  (unique items)
S5          1   S4 AND PY<=1997
S6      74685   FC
S7        125   S1 AND S6
S8     871554   FUSED OR FUSION OR CONJUGAT? OR CHIMER?
S9         79   S7 AND S8
S10        38   RD  (unique items)
S11         1   S10 AND PY<=1997
S12         0   S11 NOT S5
? s immunoglobulin
     S13  402631  IMMUNOGLOBULIN
?  s s1 and s13
           12346  S1
          402631  S13
     S14     147  S1 AND S13
```

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? s s14 and s8
             147  S14
          871554  S8
     S15      59  S14 AND S8
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
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Processing
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        33362888  PY<=1997
     S17       5  S16 AND PY<=1997
? s s17 not s5
               5  S17
               1  S5
     S18       4  S17 NOT S5
? t s18/3,k,ab/1-4

 18/3,K,AB/1     (Item 1 from file: 34)
DIALOG(R)File  34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

06124093   Genuine Article#: XW411   Number of References: 50
Title: gamma-Heregulin: a novel heregulin isoform that is an autocrine
    growth factor for the human breast cancer cell line, MDA-MB-175  (
    ABSTRACT AVAILABLE)
Author(s): Schaefer G; Fitzpatrick VD; Sliwkowski MX  (REPRINT)
Corporate Source: GENENTECH INC,/S SAN FRANCISCO//CA/94080 (REPRINT);
    GENENTECH INC,/S SAN FRANCISCO//CA/94080; UNIV FREIBURG,DEPT
    BIOL/D-7800 FREIBURG//GERMANY/
Journal: ONCOGENE,  1997 , V15, N12 (SEP 18), P1385-1394
ISSN: 0950-9232   Publication date: 19970918
Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE, HAMPSHIRE, ENGLAND RG21
    6XS
Language: English   Document Type: ARTICLE
Abstract: A novel neuregulin isoform, termed gamma-HRG, was cloned and
    characterized from the human breast cancer cell line, MDA-MB-175. As
    observed with other neuregulins, gamma-HRG, is a product of alternative
    mRNA splicing of the neuregulin gene, gamma-HRG contains the EGF-like
    and  immunoglobulin -like domains that are commonly found in other
    family members, but lacks a transmembrane and cytoplasmic region. The
    new isoform possesses a unique N-terminal region that includes a
    hydrophobic domain that may function as a secretion signal. A purified
    recombinant version of gamma-HRG competes for binding to soluble ErbB3-
    and ErbB4-IgG  fusion  proteins with affinities similar to those
    observed for rHRG beta 1(177-244). gamma-HRG has a wide distribution in
    mesenchymal or neuronal tissues but in contrast to other neuregulins,
    it is not present in breast, lung, liver and small intestine.
    Expression of gamma-HRG with its cognate receptors, ErbB3 and ErbB2
    suggested that the growth of the MDA-MB-175 cell line might be a result
    of the stimulation of a growth factor signaling pathway. Treatment of
    MDA-MB-175 cells with an anti-ErbB2 monoclonal antibody that interferes
    with the ligand-dependent formation of ErbB2-ErbB3 heterodimer
    complexes shows a strong growth inhibitory effect on this cell line.
    Moreover, incubation with a receptor-IgG  fusion  protein that
    neutralizes secreted gamma-HRG, also inhibits cell growth. These data
```

suggest that the secretion of gamma-HRG by MDA-MB-175 cells leads to the formation of a constitutively active receptor complex and stimulates the growth of these cells in an autocrine manner.

, **1997**
...Abstract: of alternative mRNA splicing of the neuregulin gene, gamma-HRG contains the EGF-like and **immunoglobulin** -like domains that are commonly found in other family members, but lacks a transmembrane and ...
...purified recombinant version of gamma-HRG competes for binding to soluble ErbB3- and ErbB4-IgG **fusion** proteins with affinities similar to those observed for rHRG beta 1(177-244). gamma-HRG...

...a strong growth inhibitory effect on this cell line. Moreover, incubation with a receptor-IgG **fusion** protein that neutralizes secreted gamma-HRG, also inhibits cell growth. These data suggest that the...
...Research Fronts: SYNTHASE EXPRESSION; ARABIDOPSIS TYPE-1 PROTEIN PHOSPHATASE)
95-8622 001 (EXPRESSION OF EPIDERMAL GROWTH-FACTOR **RECEPTOR** ; **TGF** -ALPHA AUTOCRINE LOOP; V-SIS ONCOPROTEIN LOSES TRANSFORMING ACTIVITY)

18/3,K,AB/2 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2913778 IFI Acc No: 9735086
IFI Publication Control No: 9735086
Document Type: C
RECOMBINANT ANTIBODIES FOR HUMAN THERAPY; NUCLEIC ACID SEQUENCE ENCODING OLD WORLD MONKEY IMMUNOGLOBULIN **-BINDING REGION AND SECOND SEQUENCE ENCODING HUMAN OR CHIMPANZEE REGION**
Inventors: Hanna Nabil (US); Newman Roland A (US); Raab Ronald W (US)
Assignee: IDEC Pharmaceuticals Corp
Assignee Code: 40498
Document Type: REASSIGNED
Attorney, Agent or Firm: Burns, Doane, Swecker & Mathis, LLP
Publication (No,Kind,Date), Applic (No,Date):
US 5693780 A **19971202** US 95481869 19950607
Calculated Expiration: 20141202
Priority Applic(No,Date): US 95481869 19950607; US 92912292 19920710; US 91735064 19910725; US 92856281 19920323; US 95379072 19950125

Abstract: **Chimeric** antibodies including an Old World monkey portion and a human portion, nucleic acid encoding such antibodies, Old World monkey monoclonal antibodies, and methods for their production and use.

...**NUCLEIC ACID SEQUENCE ENCODING OLD WORLD MONKEY** IMMUNOGLOBULIN **-BINDING REGION AND SECOND SEQUENCE ENCODING HUMAN OR CHIMPANZEE REGION**
Publication (No,Kind,Date), Applic (No,Date):
... **19971202**

Abstract: **Chimeric** antibodies including an Old World monkey portion and a human portion, nucleic acid encoding such...

Exemplary Claim:
...recombinant antibody which comprises (i) a first nucleic acid sequence encoding an Old World monkey **immunoglobulin** antigen-binding region and (ii) a second nucleic acid sequence encoding an **immunoglobulin** constant region selected from group consisting of human **immunoglobulin** constant region and chimpanzee **immunoglobulin** constant region.

Non-exemplary Claims:
...said recombinant antibody comprises a framework region selected from the group consisting of a human **immunoglobulin** framework region, a chimpanzee **immunoglobulin** framework region and an Old World monkey **immunoglobulin** framework region...

...wherein said antigen-binding region comprises the whole variable region of an Old World monkey **immunoglobulin** which naturally contains said Old World monkey antigen-binding portion...

...7. The nucleic acid of claim 1, wherein said Old World monkey **immunoglobulin** antigen-binding portion is specific to human CD4 and contains the VH amino acid sequence...
...receptor, CD3, CD28, CD8, CD11a, CD11b, CD18, CD5a, CD11c, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD18, CD5a, CD11c, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

18/3,K,AB/3 (Item 2 from file: 340)

Dialog Acc No: 2873822 IFI Acc No: 9722647
IFI Publication Control No: 9722647
Document Type: C
RECOMBINANT ANTIBODIES FOR HUMAN THERAPY; INCLUDES AN OLD WORLD MONKEY PORTION AND A HUMAN PORTION, NUCLEIC ACID ENCODING SUCH ANTIBODIES
Inventors: Hanna Nabil (US); Newman Roland A (US); Raab Ronald W (US)
Assignee: IDEC Pharmaceuticals Corp
Assignee Code: 40498
Document Type: REASSIGNED
Attorney, Agent or Firm: Burns, Doane, Swecker & Mathis
Publication (No,Kind,Date), Applic (No,Date):
US 5658570 A **19970819** US 95379072 19950125
Calculated Expiration: 20140819
(Cited in 006 later patents)
Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 20010327
Priority Applic(No,Date): US 95379072 19950125; US 92912292 19920710; US 91735064 19910725; US 92856281 19920323

Abstract: **Chimeric** antibodies including an Old World monkey portion and a human portion, nucleic acid encoding such antibodies, Old World monkey monoclonal antibodies, and methods for their production and use.

Publication (No,Kind,Date), Applic (No,Date):

... **19970819**

Abstract: **Chimeric** antibodies including an Old World monkey portion and a human portion, nucleic acid encoding such...

Exemplary Claim:

D R A W I N G

1. A **chimeric** antibody comprising an **immunoglobulin** constant region and an antigen binding region, said **immunoglobulin** constant region being selected from the group consisting of human **immunoglobulin** constant region and chimpanzee **immunoglobulin** constant region, and said antigen binding region being an Old World Monkey antigen-binding region.

Non-exemplary Claims:

2. A **chimeric** antibody conprising an immunoglobin variable region specific for a particular known antigen, said antibody comprising...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD18, CD5a, CD11c, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CD5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD11a, CD11b, CD11c, CD18, CD5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...17. The method of claim 15 wherein said immortalizing is by hybridoma **fusion** .

claim 12 wherein said isolating comprises **immunoglobulin** gene rescue of said variable region...

...receptor, CD3, CD28, CD8, CD18, CD11a, CD11b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, and CD71...

...receptor, CD3, CD28, CD8, CD18, CD11a, CD11b, CD11c, C5a, CD45, neu oncogene product, MDR-1, **TGF** Alpha , **TGF** Alpha **receptor** , PDGF, or CD71...

4/3,K,AB/4256 (Item 190 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2338038 IFI Acc No: 9305038
IFI Publication Control No: 9305038
Document Type: C
METHOD FOR USING SYNTHETIC ANALOGS OF THROMBOSPONDIN **FOR** INHIBITING **METASTASIS ACTIVITY**
Inventors: Eyal Jacob (US); Hamilton Bruce K (US); Tuszynski George P (US)
Assignee: Grace, W R & Co-Conn
Assignee Code: 20513
Attorney, Agent or Firm: Appleby, Vanessa L; Krafte, Jill H; Trinker, Steven T
Publication (No,Kind,Date), Applic (No,Date):
US 5190920 A 19930302 US 90587197 19900924
Calculated Expiration: 20100924
(Cited in 019 later patents)
Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19940111, 19940308
Priority Applic(No,Date): US 90587197 19900924

Abstract: Compounds and compositions comprising fragments and methods for using synthetic analogs of **thrombospondin** for promoting or inhbiting **thrombospondin** -like activity are provided.

METHOD FOR USING SYNTHETIC ANALOGS OF THROMBOSPONDIN **FOR** INHIBITING **METASTASIS ACTIVITY**

Abstract: Compounds and compositions comprising fragments and methods for using synthetic analogs of **thrombospondin** for promoting or inhbiting **thrombospondin** -like activity are provided.

Exemplary Claim:
1. A method for **inhibiting** metastasis comprising administering to an animal an effective amount of a polypeptide compound of the...
Non-exemplary Claims:
...of: CSVTCG CSVTCG-NH2 CSVTCG (disulfide linked) CSTSCG CSTSCG-NH2 CSTSCG (disulfide linked) CSTSCG-NH2 (**blocked** Cys residues) CRVTCG CRVTCG (disulfide linked) CRVTCG-NH2 RCRVTCG (disulfide linked) CSVTCK CSVTCR-NH2 CSRTCG...

...3. The method of claim 1 which **inhibits** tumor cell metastasis...

...4. The method of claim 1 which **inhibits** tumor growth...

...7. The method of claim 1 which **inhibits** adhesion of tumor cells...

4/3,K,AB/4257 (Item 191 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 2338036 IFI Acc No: 9305036
IFI Publication Control No: 9305036
Document Type: C
PEPTIDE FRAGMENTS AND ANALOGS OF THROMBOSPONDIN **AND METHODS OF USE;**

ANTITUMOR
Inventors: Deutch Alan H (US); Tuszynski George (US)
Assignee: Grace, W R & Co-Conn; Medical College of Pennsylvania
Assignee Code: 20513 29291
Attorney, Agent or Firm: Appleby, Vanessa L; Krafte, Jill H; Trinker, Steven T
Publication (No,Kind,Date), Applic (No,Date):
US 5190918 A 19930302 US 90483527 19900222
Calculated Expiration: 20100302
(Cited in 018 later patents)
Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19961008
Priority Applic(No,Date): US 90483527 19900222

Abstract: Compounds and compositions comprising fragments and synthetic analogs of human **thrombospondin** are provided together with methods for their use as **thrombospondin** -like agents.

PEPTIDE FRAGMENTS AND ANALOGS OF THROMBOSPONDIN **AND METHODS OF USE...**

Abstract: Compounds and compositions comprising fragments and synthetic analogs of human **thrombospondin** are provided together with methods for their use as **thrombospondin** -like agents.

Exemplary Claim:

D R A W I N G

1. A method for **inhibiting** tumor metastatic activity comprising administering an effective amount of a polypeptide compound having the formula...

Non-exemplary Claims:

...3. The method of claim 1 which **inhibits** or prevents pulmonary metastasis...

...4. The method of claim 1 which **inhibits** or prevents adhesion of tumor cells...

...5. The method of claim 4 wherein said tumor cells are responsive to **thrombospondin** .

?

Regulation of transforming growth factor-beta activation by discrete sequences of thrombospondin **1.**

Schultz-Cherry S; Chen H; Mosher D F; Misenheimer T M; Krutzsch H C; Roberts D D; Murphy-Ullrich J E

Department of Pathology, University of Alabama at Birmingham 35294-0019, USA.

Journal of biological chemistry (UNITED STATES) Mar 31 **1995** , 270 (13) p7304-10, ISSN 0021-9258--Print Journal Code: 2985121R

Contract/Grant No.: HL08640; HL; NHLBI; HL49111; HL; NHLBI; HL50061; HL; NHLBI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Transforming growth factor-beta (TGF-beta) is a potent growth regulatory protein secreted by virtually all cells in a latent form. A major mechanism of regulating TGF-beta activity occurs through factors that control the processing of the latent to the biologically active form of the molecule. We have shown previously that **thrombospondin** 1 (TSP1), a platelet alpha-granule and extracellular matrix protein, activates latent TGF-beta via a protease- and cell-independent mechanism and have localized the TGF-beta binding/activation region to the type 1 repeats of platelet TSP1. We now report that recombinant human TSP1, but not recombinant mouse TSP2, activates latent TGF-beta. Activation was further localized to the unique sequence RFK found between the first and the second type 1 repeats of TSP1 (amino acids 412-415) by the use of synthetic peptides. A peptide with the corresponding sequence in TSP2, RIR, was inactive. In addition, a hexapeptide GGWSHW, based on a sequence present in the type 1 repeats of both TSP1 and TSP2, **inhibited** the activation of latent **TGF** -beta by TSP1. This peptide bound to 125I-active **TGF** -beta and **inhibited** interactions of TSP1 with latent **TGF** -beta. TSP2

? ds

Set	Items	Description
S1	19	THROMBOSPONDIN (W)PEPTIDE
S2	9859	THROMBOSPONDIN
S3	4480591	INHIBIT? OR BLOCK? OR ANTAGON? (5N)TGF?
S4	4257	S2 AND S3
S5	19277	(INHIBIT? OR BLOCK? OR ANTAGON?) (5N)TGF?
S6	2327288	BIND?
S7	255	S2 AND S5
S8	125	RD (unique items)
S9	20	S8 AND PY<=1997
S10	18	S9 AND PY<1997

? t s10/3,k,ab/1-18

10/3,K,AB/1 (Item 1 from file: 155)

11149546 PMID: 8979269

Clonal variation of p53 expression and proliferative phenotype in A253 squamous carcinoma cells.

Galbraith S C; Foley J; Kats Y; Moy A; Dann P; Burtis W J; Philbrick W M; Orloff J J

Division of Endocrinology and Metabolism, VA Connecticut Healthcare System, West Haven, CT 06516, USA.

Oncology research (UNITED STATES) **1996** , 8 (9) p353-61, ISSN 0965-0407--Print Journal Code: 9208097

Contract/Grant No.: CA-16359; CA; NCI; CA-63765; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Loss of normal p53 tumor-suppressor gene function is characteristic of the majority of squamous carcinomas. During the course of gene transfer studies in the human squamous carcinoma cell line, A253, which does not express p53 mRNA or protein, we incidentally observed increased levels of p53 expression in up to 20% of clonal cell lines derived from parental A253 cells. p 53-expressing A253 cells (A253-p53) were also isolated by dilutional cloning. Nuclear p53 protein was identified by immunohistochemistry in A253-p53 cells in a wild-type pattern, and p53 mRNA (2.5 kb) was demonstrated by northern blot. Mutational analysis of the p53 gene in A253-p53 cells revealed no evidence for mutations in exons 5-9. A253-p53 cells could be distinguished from native A253 cells by prolonged doubling times (2-5 fold) and by a marked reduction of [3H]-thymidine uptake. Whereas A253 cells were unresponsive to the growth- **inhibitory** effects of **TGF** -beta, EGF-stimulated A253-p53 cells responded to TGF-beta with markedly reduced DNA synthetic rates. A253-p53 cells cocultured with A253 demonstrated enhanced cell growth and DNA synthesis rates compared to control A253-p53 cells. Finally, A253-p53 cells show reduced expression of c-fos, fibronectin, **thrombospondin** and parathyroid hormone-related protein (PTHrP) mRNAs. PTHrP measured by RIA in conditioned medium was approximately 300 pM for A253 but undetectable for A253-p53. We conclude that the A253 cell line contains a subpopulation of cells which express high levels of "wild-type-like" p53 protein. This results in dramatic changes in gene expression and a slower-growing phenotype in vitro.

... **1996** ,

... a marked reduction of [3H]-thymidine uptake. Whereas A253 cells were unresponsive to the growth- **inhibitory** effects of **TGF** -beta, EGF-stimulated A253-p53 cells responded to TGF-beta with markedly reduced DNA synthetic...

... control A253-p53 cells. Finally, A253-p53 cells show reduced expression of c-fos, fibronectin, **thrombospondin** and parathyroid hormone-related protein (PTHrP) mRNAs. PTHrP measured by RIA in conditioned medium was...

10/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11130203 PMID: 8954178
Transforming growth factor-beta: a general review.
Lawrence D A
Growth Factors Group, UMR 146 du CNRS, Institut Curie, Orsay, France.
European cytokine network (FRANCE) Sep **1996** , 7 (3) p363-74, ISSN 1148-5493--Print Journal Code: 9100879
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Three isoforms of Transforming Growth Factor-beta (TGF-beta 1, beta 2 and beta 3) exist in mammals. They play critical roles in growth regulation and development. Each isoform is encoded by a unique gene on different chromosomes. All three of these growth factors are secreted by most cell types, generally in a latent form, requiring activation before they can exert biological activity. This activation of latent TGF-beta, which may involve plasmin, **thrombospondin** and possibly acidic microenvironments, appears to be a crucial regulatory step in controlling their effects. The TGF-betas possess three major activities: they inhibit proliferation of most cells, but can stimulate the growth of some mesenchymal cells; they exert immunosuppressive effects; and they enhance the formation of extracellular matrix. Two types of membrane receptors (type I and type II) possessing a serine/threonine kinase activity within their cytoplasmic domains are involved in signal transduction. **Inhibition** of growth by the **TGF** -betas stems from a **blockage** of the cell cycle in late G1 phase. Among the molecular participants concerned in G1-arrest are the Retinoblastoma (Rb) protein and members of the Cyclin/Cyclin-dependent kinase/Cyclin dependent kinase inhibitor families. In the intact organism the TGF-betas are involved in wound repair processes and in starting inflammatory reactions and then in their resolution. The latter effects of the TGF-betas derive in part from their chemotactic attraction of inflammatory cells and of fibroblasts. From gene knockout and from overexpression studies it has been shown that precise regulation of each isoform is essential for survival, at least in the long term. Several clinical applications for certain isoforms have already shown their efficacy and they have been implicated in numerous other pathological situations.

... **1996** ,
... they can exert biological activity. This activation of latent TGF-beta, which may involve plasmin, **thrombospondin** and possibly acidic microenvironments, appears to be a crucial regulatory step in controlling their effects...

... possessing a serine/threonine kinase activity within their cytoplasmic domains are involved in signal transduction. **Inhibition** of growth by the **TGF** -betas stems from a **blockage** of the cell cycle in late G1 phase. Among the molecular participants concerned in G1...

10/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10959019 PMID: 8728286
[Transforming growth factor-beta and its receptors]
Miyazono K
Department of Biochemistry, Cancer Institute, Tokyo, Japan.
Nippon yakurigaku zasshi. Folia pharmacologica Japonica (JAPAN) Mar **1996** , 107 (3) p133-40, ISSN 0015-5691--Print Journal Code: 0420550
Publishing Model Print
Document type: Journal Article; Review ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Transforming growth factor-beta (TGF-beta) is a family of multifunctional proteins that inhibit the growth of most cell types, and these proteins induce the deposition of extracellular matrix. **TGF** -beta **inhibits** the growth and migration of endothelial cells in vitro, but induces angiogenesis in vivo. TGF-beta belongs to a larger superfamily known as the TGF-beta superfamily, which includes activins and bone morphogenetic proteins. TGF-beta is produced as latent high molecular weight complexes from producer cells and is then activated by plasmin or **thrombospondin** . Latent TGF-beta binding protein (LTBP) is a component of the latent TGF-beta complex produced from platelets and many other cell types; LTBP plays an important role for the interaction of the latent TGF-beta complex with extracellular matrix components. TGF-beta binds several cell surface receptors, including type III receptor (betaglycan), endoglin, type II receptor and type I receptor. The type III receptor and endoglin are indirectly involved in the signal transduction. The Type II and type I receptors have intracellular serine/threonine kinase domains. They form a heteromeric complex after ligand binding and are most important for signal transduction; the type II receptor transactivates the type I receptor, which transduces various signals.

... **1996** ,
... the growth of most cell types, and these proteins induce the deposition of extracellular matrix. **TGF** -beta **inhibits** the growth and migration of endothelial cells in vitro, but induces angiogenesis in vivo. TGF...

... latent high molecular weight complexes from producer cells and is then activated by plasmin or **thrombospondin** . Latent TGF-beta binding protein (LTBP) is a component of the latent TGF-beta complex...

10/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10794558 PMID: 8557772
Induction of transforming growth factor-beta autocrine activity by

all-trans-retinoic acid and 1 alpha,25-dihydroxyvitamin D3 in NRP-152 rat prostatic epithelial cells.

Danielpour D

Laboratory of Chemoprevention, National Cancer Institute, Bethesda, Maryland 20892, USA.

```
Set     Items   Description
S1      51208   PAPILLOMAVIRUS
S2    3145781   CANCER OR TUMOR OR MALIGNAN?
S3      31221   S1 AND S2
S4    8475576   TREAT? OR INHIBIT?
S5       8087   S3 AND S4
S6      13923   TYPE(W)16
S7       3107   S5 AND S6
S8        808   PAPILLOMAVIRUS (5N)ANTIGEN
S9        388   S8 AND PY<=1997
S10       289   RD  (unique items)
S11    337618   CERVI?
S12        99   S10 AND S11
S13    103299   TGF?
S14         1   S12 AND S13
? s adjuvant or detergent
          162476  ADJUVANT
           75429  DETERGENT
     S15  237493  ADJUVANT OR DETERGENT
? s s12 and s15
              99  S12
          237493  S15
     S16       2  S12 AND S15
? t s16/3,k,ab/1-2

 16/3,K,AB/1     (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2006 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 2916131  IFI Acc No: 9735480
IFI Publication Control No: 9735480
Document Type: C
INDUCTION OF CYTOTOXIC T-LYMPHOCYTE RESPONSES
Inventors: Black Amelia (US); Rastetter William H (US); Raychaudhuri Syamal
    (US)
Assignee: IDEC Pharmaceuticals Corp
Assignee Code: 40498
Document Type: REASSIGNED
Attorney, Agent or Firm: Burns, Doane, Swecker & Mathis, LLP
Publication (No,Kind,Date), Applic (No,Date):
US 5695770     A   19971209  US 95472311    19950607
Calculated Expiration: 20141209
   (Cited in 004 later patents)
Priority Applic(No,Date): US 95472311     19950607; US 94351001
19941207; US 91735069     19910725; US 92919787     19920724

Abstract: Methods and compositions useful for inducing a cytotoxic T
lymphocyte response (CTL) in a human or domesticated or agriculturally
important animal. The method includes the steps of providing the antigen to
which the CTL response is desired and providing an antigen formulation
which comprises, consists, or consists essentially of two or more of a
stabilizing  detergent , a micelle-forming agent, and an oil. This antigen
formulation is preferably lacking in an immunostimulating peptide
component, or has sufficiently low levels of such a component that the
desired CTL response is not diminished. This formulation is provided as a
stable oil-in-water emulsion.


Publication (No,Kind,Date), Applic (No,Date):
```

... **19971209**

Abstract: ...antigen formulation which comprises, consists, or consists essentially of two or more of a stabilizing **detergent** , a micelle-forming agent, and an oil. This antigen formulation is preferably lacking in an...

Exemplary Claim:

D R A W I N G

1. A composition comprising a **papillomavirus antigen** mixed with a microfluidized **antigen** formulation comprising: (a) a stabilizing **detergent** , (b) a micelie-forming agent, and (c) a biodegradable and biocompatible oil, said antigen formulation...

...animals and agricultural animals is capable of inducing a specific cytotoxic Tlymphocyte response against the **papillomavirus antigen** contained in the composition.

Non-exemplary Claims:

2. The composition of claim 1, wherein said **papillomavirus antigen** is selected from the group consisting of HPV16 E6 antigen, HPV16 E7 antigen, HPV18 E6...

...3. A method for treating **cervical** cancer comprising administering a therapeutically effective amount of a human **papillomavirus antigen** formulation according to claim 2...

...A method for treating condyloma acuminata comprising administering a therapeutically effective amount of a human **papillomavirus antigen** formulation according to claim 2...

...5. The composition of claim 1, wherein the **detergent** is selected from the group consisting of Tween 20, Tween 40 and Tween 80; the...

...6. The composition of claim 1, wherein the **detergent** is polysorbate 80, and the micelle-forming agent is polyoxamer 401...

...7. The composition of claim 1, wherein the **detergent** is selected from the group consisting of polysorbate 80, Tween 20, Tween 40, Tween 60...

16/3,K,AB/2 (Item 2 from file: 340)

Dialog Acc No: 1855352 IFI Acc No: 8809712
IFI Publication Control No: 8809712
Document Type: C

ASSAY METHOD AND REAGENT TO DETERMINE ANTIBODIES TO PAPILLOMAVIRUS VIRIONS

Inventors: BAIRD PHILLIP J (AU)
Assignee: UNASSIGNED OR ASSIGNED TO INDIVIDUAL
Assignee Code: 68000
Publication (No,Kind,Date), Applic (No,Date):
US 4748109 A **19880531** US 84626777 19840702
Calculated Expiration: 20050531
(Cited in 025 later patents) **Document Type: EXPIRED**
Priority Applic(No,Date): AU 8383 19830701

Abstract: The invention provides a reagent and assay to detect, inter alia

anogenital warts, **cervical** intraepithelial neoplasia and invasive squamous cell carcinoma of the uterine **cervix** using disrupted **Papillomavirus** virions or **antigen** extract thereof.

Publication (No,Kind,Date), Applic (No,Date):
... **19880531**

Abstract: The invention provides a reagent and assay to detect, inter alia anogenital warts, **cervical** intraepithelial neoplasia and invasive squamous cell carcinoma of the uterine **cervix** using disrupted **Papillomavirus** virions or **antigen** extract thereof.

Exemplary Claim:

1. A REAGENT USEFUL IN THE DETECTION OF ANOGENITAL WARTS, **CERVICAL** INTRAEPITHELIAL NEOPLASIA AND **CERVICAL** SQUAMOUS CARCINOMA, SAID REAGENT COMPRISING A SOLID OR PARTICULATE SUPPORT COATED WITH PROTEINS OF DISRUPTED **PAPILLOMAVIRUS** VIRIONS, OR **ANTIGEN** EXTRACT THEREOF.

Non-exemplary Claims:

...of claim 1 or 2 wherein said Papillomavirus virions are bovine, human, rabbit or horse **papillomavirus** virions or **antigen** extract thereof...

...7. A method for preparing a diagnostic reagent useful in the detection of anogenital warts, **cervical** intraepithelial neoplasia and **cervical** squamous carcinoma, said method comprising the steps of; (1) contacting a solid particulate support with disrupted **Papillomavirus** virions or an **antigen** extract thereof; (2) incubating said support with said virions or extract for a time and...

...means, the virus particles isolated, and said particles are disrupted by contact with a surfactant, **detergent** or effective salt concentration ...

...12. A method for the detection of anogenital warts, **Cervical** intraepithelial neoplasia (CIN) and invasive squamous cell carcinoma of the uterine **cervix** , said method comprising the steps of: (1) providing a solid or particulate support coated with proteins of disrupted **Papillomavirus** virions or an **antigen** extract thereof; (2) contacting said coated support with an aliquot of a body fluid under...

...of claims 12 or 17 wherein said Papillomavirus virions are bovine, human, rabbit, or horse **Papillomavirus** virions or **antigen** extract thereof...

?

HLA-A2-restricted peripheral blood cytolytic T lymphocyte response to HPV type 16 proteins E6 and E7 from patients with neoplastic cervical **lesions.**

Evans C; Bauer S; Grubert T; Brucker C; Baur S; Heeg K; Wagner H; Lipford G B

Institute for Medical Microbiology, Technical University of Munich, Germany.

Cancer immunology, immunotherapy - CII (GERMANY) Mar **1996** , 42 (3) p151-60, ISSN 0340-7004--Print Journal Code: 8605732

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The DNA from human papillomavirus (HPV) can be detected in 90% of **cervical** carcinomas. To address whether patients infected with HPV can mount efficient T cell responses to this pathogen we examined the cytotoxic T lymphocyte (CTL) response of peripheral blood mononuclear cells (PBMC) from patients with abnormal genital epithelial cells. PBMC from 11 HLA-A2+ patients were stimulated with CaSki, a **cervical** carcinoma cell line that is HPV 16+ and HLA-A2+. The CTL were screened for reactivity to the **cervical** carcinoma cell line C33A (HPV-, HLA-A2+) transfected with the HPV 16 E6 or E7 genes or the plasmid without insert. The CTL of 1 patient showed particularly strong CaSki and HPV E6 or E7 protein-specific cytotoxicity in a HLA-A2+-restricted fashion. In contrast, these CTL lysed neither a vector-only transfectant, the natural killer cell (NK) target, K562 nor the lymphokine-activated killer cell (LAK) target, Daudi. HLA-A2 restriction was demonstrated by the lack of recognition of a HLA-A2- CaSki cell line developed in our laboratory. The CTL line was cloned and 99 clones were harvested and screened; 51 clones lysed CaSki, of which 17 did not lyse the A2- CaSki. Of these HLA-A2- restricted clones, 8 did not lyse C33A transfectants, 6 lysed all C33A transfectants, 3 lysed C33A-E7 only and none lysed C33A-E6 only. These data imply that, within the bulk CTL line, HLA-A2-restricted recognition of antigens was restricted to CaSki antigens, antigens common to **cervical** carcinoma (CaSki plus C33A), or HPV-16-E7-derived antigen on the clonal level. The E7-restricted clones were negative for recognition of known HLA-A2-binding peptides from E7.

...**T lymphocyte response to HPV type 16 proteins E6 and E7 from patients with neoplastic** cervical **lesions.**

... **1996** ,

The DNA from human papillo

eneration of tumor-specific cytolytic T lymphocytes from peripheral blood of cervical **cancer patients by in vitro stimulation with a synthetic human papillomavirus type 16 E7 epitope.**

Alexander M; Salgaller M L; Celis E; Sette A; Barnes W A; Rosenberg S A; Steller M A

Surgery Branch, National Cancer Institute, Bethesda, MD 20892-1502, USA.

American journal of obstetrics and gynecology (UNITED STATES) Dec **1996**, 175 (6) p1586-93, ISSN 0002-9378--Print Journal Code: 0370476

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

OBJECTIVE: Approximately 90% of squamous carcinomas of the **cervix** harbor the human papillomavirus and type 16 has been detected in nearly 50% of cases. Recent studies in mice have shown that the human papillomavirus type 16 E7 oncoprotein contains peptide epitopes that are processed and presented in association with a major histocompatibility antigen for recognition by cytolytic T lymphocytes. We investigated whether an epitope from human papillomavirus type 16 E7 could be used to generate specific human cytolytic T lymphocytes in patients with **cervical** carcinoma. STUDY DESIGN: After radiation therapy, three patients with antigen HLA-A2 and with locally advanced **cervical** cancer underwent leukapheresis. Epitope-specific cytolytic T lymphocytes were generated from the peripheral blood mononuclear cells by in vitro stimulation with autologous peripheral blood mononuclear cells pulsed with a human papillomavirus type 16 E7, HLA-A2-restricted, synthetic peptide, E7(11-20) (YMLDLQPETT). RESULTS: In two patients cytolytic T lymphocytes were capable of E7(11-20)-specific, HLA-A2-restricted cytolysis of the peptide-pulsed, HLA-matched, T2 target cell line. Cytolytic T lymphocytes from one of these patients also demonstrated specific cytolysis against the HLA-A2+, HPV-16+ CaSki **cervical** cancer cell line but did not lyse either HLA-A2+, HPV-16- MS-751 cells or HLA-A2-, HPV-16- HT-3 cells. CONCLUSIONS: These experiments demonstrate that novel cytolytic T lymphocytes that recognize a human papillomavirus type 16 E7 epitope can be generated by using the peripheral blood mononuclear cells from irradiated patients with **cervical** cancer. In addition, because CaSki cells were specifically lysed by the cytolytic T lymphocytes, these data indicate that the peptide E7(11-20) is endogenously processed and presented on the cell surface of the CaSki cells. The demonstration of epitope-specific lysis of cytolytic T lymphocytes of HPV-16+ **cervical** cancer cells supports further efforts to develop human **papillomavirus** peptide-based vaccines or **antigen** -specific

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Set     Items   Description
S1      51208   PAPILLOMAVIRUS
S2    3145781   CANCER OR TUMOR OR MALIGNAN?
S3      31221   S1 AND S2
S4    8475576   TREAT? OR INHIBIT?
S5       8087   S3 AND S4
S6      13923   TYPE(W)16
S7       3107   S5 AND S6
S8        808   PAPILLOMAVIRUS (5N)ANTIGEN
S9        388   S8 AND PY<=1997
S10       289   RD  (unique items)
S11    337618   CERVI?
S12        99   S10 AND S11
? s tgf?
     S13  103299  TGF?
? s s12 and s13
             99  S12
         103299  S13
     S14       1  S12 AND S13
? t s14/3,k,ab/1

 14/3,K,AB/1     (Item 1 from file: 34)
DIALOG(R)File  34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

02975937   Genuine Article#: MW686   Number of References: 54
Title: TRANSFORMING GROWTH-FACTOR-BETA-1 REGULATION OF METALLOPROTEINASE
    PRODUCTION IN CULTURED HUMAN  CERVICAL  EPITHELIAL-CELLS  (Abstract
    Available)
Author(s): AGARWAL C; HEMBREE JR; RORKE EA; ECKERT RL
Corporate Source: CASE WESTERN RESERVE UNIV,SCH MED,DEPT PHYSIOL &
    BIOPHYS,ROOM E532,2109 ADELBERT RD/CLEVELAND//OH/44106; CASE WESTERN
    RESERVE UNIV,SCH MED,DEPT PHYSIOL & BIOPHYS/CLEVELAND//OH/44106; CASE
    WESTERN RESERVE UNIV,SCH MED,DEPT BIOCHEM/CLEVELAND//OH/44106; CASE
    WESTERN RESERVE UNIV,SCH MED,DEPT REPROD BIOL/CLEVELAND//OH/44106; CASE
    WESTERN RESERVE UNIV,SCH MED,DEPT DERMATOL/CLEVELAND//OH/44106; CASE
    WESTERN RESERVE UNIV,SCH MED,DEPT ENVIRONMHLTH SCI/CLEVELAND//OH/44106
Journal: CANCER RESEARCH,  1994 , V54, N4 (FEB 15), P943-949
ISSN: 0008-5472
Language: ENGLISH   Document Type: ARTICLE
Abstract: Collagenase levels are regulated in a cell type-specific manner
    by a variety of growth factors and cytokines, and increased type IV
    collagenase activity in tumor cells has been linked to metastatic
    growth. In this study we compare the effects of epidermal growth factor
    (EGF) and transforming growth factor beta 1 ( TGF  beta 1) on
    gelatinase production in  cervical  epithelial cell lines. EGF is a
    strong mitogen for  cervical  epithelial cells and  TGF  beta 1
    suppresses growth. Metalloproteinase zymograms of conditioned medium
    from normal human ectocervical cells reveal two major bands of
    metalloproteinase activity at 72 and 92 Kd. In contrast, the level of
    the 92-Kd activity is greatly reduced in the human papillomavirus type
    16-positive ECE16-1 and CaSki cells. EGF treatment produces minimal
    changes in metalloproteinase levels. Treatment of CaSki cells with 20
    ng/ml of EGF reduces by 30 to 50% the level of both activities. In
    ECE16-1 cells, EGF decreases the 72-Kd activity by 50% and the 92-Kd
    activity slightly.  TGF  beta 1 treatment, in contrast, increases the
    72-Kd activity 3- to 10-fold and the 92-Kd activity by greater than or
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08/4/06

equal to 25-fold in each cell type. In CaSki and ECE16-1 cells, the changes in metalloproteinase level are mediated by changes in level of the corresponding mRNAs. In each case, the metalloproteinases are secreted as inactive proenzymes which can be activated by in vitro treatment with organomercurials. Tests of a series of additional **cervical** cell lines reveal that metalloproteinase levels are generally higher in normal **cervical** cells and in cells immortalized by transfection with HPV16, whereas lower levels are observed in cells derived from human tumors. Moreover, a higher percentage of cell lines derived from human tumors do not respond to **TGF** beta 1 regulation of metalloproteinase levels. Parallel studies indicate that the **TGF** beta 1-stimulated increase in the 72- and 92-Kd activities is correlated with enhanced chemotactic and chemoinvasive behavior in both ECE16-1 and CaSki cells.

Title: TRANSFORMING GROWTH-FACTOR-BETA-1 REGULATION OF METALLOPROTEINASE PRODUCTION IN CULTURED HUMAN CERVICAL **EPITHELIAL-CELLS**
, 1994

...Abstract: we compare the effects of epidermal growth factor (EGF) and transforming growth factor beta 1 (**TGF** beta 1) on gelatinase production in **cervical** epithelial cell lines. EGF is a strong mitogen for **cervical** epithelial cells and **TGF** beta 1 suppresses growth. Metalloproteinase zymograms of conditioned medium from normal human ectocervical cells reveal...

...cells, EGF decreases the 72-Kd activity by 50% and the 92-Kd activity slightly. **TGF** beta 1 treatment, in contrast, increases the 72-Kd activity 3- to 10-fold and...

...can be activated by in vitro treatment with organomercurials. Tests of a series of additional **cervical** cell lines reveal that metalloproteinase levels are generally higher in normal **cervical** cells and in cells immortalized by transfection with HPV16, whereas lower levels are observed in...

...Moreover, a higher percentage of cell lines derived from human tumors do not respond to **TGF** beta 1 regulation of metalloproteinase levels. Parallel studies indicate that the **TGF** beta 1-stimulated increase in the 72- and 92-Kd activities is correlated with enhanced...

...Research Fronts: EXPRESSION; MUSCLE OF KURUMA PRAWN PENAEUS-JAPONICUS; PARTIAL CDNA FOR MOUSE 180-KDA BULLOUS PEMPHIGOID **ANTIGEN** (BPAG2))
92-8345 001 (HUMAN **PAPILLOMAVIRUS** TYPE-16 DNA; **CERVICAL** INTRAEPITHELIAL NEOPLASIA; SQUAMOUS-CELL CARCINOMA; POLYMERASE CHAIN-REACTION)

?